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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/759,731	01/16/2004	Christopher J. Bond	11669.136USU1	6901

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EXAMINER	
STEELE, AMBER D	

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
08/21/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/759,731	BOND, CHRISTOPHER J.	
	Examiner	Art Unit	
	AMBER D. STEELE	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *June 15, 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *105-107,109-111,113-128* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-7,9-12,15,16,18-24,29-34,36-40,42,44-46,48-54,59-66,68-74,76,81-85,90-96,98,99 and 105-130.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 1-7,9-12,15,16,18-24,29-34,36-40,42,44-46,48-54,59-66,68-74,76,81-85,90-96,98,99,108,112,129 and 130.

DETAILED ACTION

1. Please note: the examiner of record for the present application has changed. However, the Technology Center (TC1600) and Art Unit (AU1639) remain the same.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 15, 2009 has been entered.

Status of the Claims

3. Claims 1-114 were originally filed on January 16, 2004.

The preliminary amendment received on October 8, 2004 amended claims 3-6, 15-16, 22, 25, 29, 45, 52, 55, 62-66, 68, 70, 77, 84-85, 94, 102, and 105 and canceled claims 8, 13-14, 17, 35, 41, 43, 47, 67, 75, 86-89, 97, and 100-101.

The amendment received on August 27, 2007 canceled claims 25-28, 55-58, 77-80, and 102-104, amended claims 105-114, and added new claims 115-130.

The amendment received on May 30, 2008 amended claims 105-111, 121-123, 126, and 127.

The amendment received on November 19, 2008 amended claim 123.

The amendment received on June 15, 2009 amended claims 105, 115, and 123.

Claims 1-7,9-12,15,16,18-24,29-34,36-40,42,44-46,48-54,59-66,68-74,76,81-85,90-96,98,99, and 105-130 are currently pending.

Claims 105-107, 109-111, and 113-128 are currently under consideration.

Election/Restrictions

4. Applicants elected, without traverse, Group I in the reply filed on November 13, 2006. Applicants elected, without traverse, the species of CDRH3 scaffold, N-terminal sequence of RIGR, and C-terminal sequence of WVTW in the reply filed on November 13, 2006. Claims 1-7, 9-12, 15-16, 18-34, 36-40, 42, 44-46, 48-66, 68-74, 76-85, 90-96, 98-99, and 102-104 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

Rejoinder

5. Applicants have requested rejoinder of all pending claims after a Notice of Allowance is issued. While applicants did elect product claims, additional product claims will not be rejoined. In addition, it is noted that rejoinder of process claims is only for process claims that depend from or otherwise include all the limitations of the allowable product claims (see MPEP § 821.04 and the "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996)). Furthermore, in order to retain the right to rejoinder in accordance with the above policy, applicant should amend the process claims during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Applicants have failed to amend the process claims during prosecution and therefore have lost the right to a rejoinder.

Priority

6. The present application claims the benefit of U.S. provisional applications 60/441,059 filed January 16, 2003; 60/488,610 filed July 18, 2003; and 60/510,314 filed October 8, 2003.

7. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the prior application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See Transco Prods., Inc. v. Performance Contracting, Inc., 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994) [taken from MPEP 201.01]

Provisional applications 60/441,059; 60/488,610; and 60/510,314 do not have support for a CDRH3-phage coat fusion protein comprising an "N-terminal portion of 1 to 4 amino acids in which some or all amino acid positions are structural"; "a C terminal portion of 1 to 6 amino acids in which some or all amino acid positions are structural"; and "a portion of a filamentous phage coat protein wherein the portion of the phage coat protein provides for display of the fusion protein on the filamentous phage".

Therefore January 16, 2004 remains the date for the purposes of prior art concerning claims 105-107, 109-111, and 113-128.

Arguments and Response

8. Applicants' arguments directed to the priority date for claims 105-107, 109-111, and 113-128 were considered but are not persuasive for the following reasons.

Applicants contend that provisional applications 60/441,059; 60/488,610; and 60/510,314 provide support for an "N-terminal portion of 1 to 4 amino acids in which some or all amino acid positions are structural" and a "portion of a filamentous phage coat protein wherein the portion of the phage coat protein provides for display of the fusion protein on the filamentous phage". Applicants also point to Figures 45 and 46 and pages 18, 21, 33, 68, and 107 of 60/441,059 and pages 18, 22, 109, and 113 of 60/488,610.

Applicants' arguments are not convincing since provisional applications 60/441,059; 60/488,610; and 60/510,314 do not provide support for an "N-terminal portion of 1 to 4 amino acids in which some or all amino acid positions are structural" and a "portion of a filamentous phage coat protein wherein the portion of the phage coat protein provides for display of the fusion protein on the filamentous phage". Pages 18 of 60/441,059; 60/488,610; and 60/510,314 state that "[s]tructural amino acid positions are selected from the group consisting of the first N-terminal amino acid and the second N-terminal amino acid" (i.e. one N-terminal structural amino acid wherein either the first or second N-terminal amino acid is structural, not "1 to 4 amino acids in which some or all amino acid positions are structural"; residues 3 and 4 are not disclosed as being structural). Provisional applications 60/441,059; 60/488,610; and 60/510,314 also do not provide support for a fusion protein wherein both the N-terminus and the C-terminus comprises structural amino acids (i.e. see "selected from the consisting of" language utilized in the specifications regarding the structural positions for either the first N-terminal amino acid, the second N-terminal amino acid, or any of the 6 C-terminal amino acids).

In addition, provisional applications 60/441,059; 60/488,610; and 60/510,314 do not disclose the minimal requirements for "a portion of a filamentous phage coat protein wherein the

portion of the phage coat protein provides for display of the fusion protein on the filamentous phage" (i.e. minimum requirements of the filamentous phage coat protein necessary for display of the fusion protein on filamentous phage). Provisional applications 60/441,059; 60/488,610; and 60/510,314 disclose gene III and gene VII (i.e. full length filamentous phage coat proteins). While "or portion thereof" is also disclosed, the minimal requirements for display of the fusion protein on filamentous phage are not disclosed.

Invention as Claimed

9. A fusion protein comprising at least a portion of a filamentous phage coat protein fused to a binding polypeptide comprising a heavy chain variable domain comprising a CDRH3 scaffold comprising (a) an N-terminal portion of 1 to 4 amino acids in which some or all amino acid positions are structural; (b) a C terminal portion of 1 to 6 amino acids in which some or all amino acid positions are structural; and (c) a central portion or loop of 1 to 20 contiguous amino acids that can vary in sequence and in length wherein the portion of the phage coat protein provides for display of the fusion protein on the filamentous phage and variations thereof.

10. The structure required by the present claims is a fusion protein comprising (a) a portion of a filamentous phage coat protein and (b) CDRH3 wherein the CDRH3 comprises (i) an N-terminal portion of 1 to 4 amino acids, (ii) a C-terminal portion of 1 to 6 amino acids, and (iii) a central portion or loop of 1 to 20 amino acids. Therefore, any fusion protein comprising at least a portion of a filamentous phage coat protein and a CDRH3 comprising from three to thirty amino acids reads on the presently claimed invention.

Invention in the Specification

11. It is noted that the specification discloses the following at page 7:

> In some embodiments, the length of the N-terminal flanking region is at least about from 1 to 4 contiguous amino acids, the central portion of at least one non-structural position(s) can vary from about 1 to 20 contiguous amino acids, and the C-terminal portion is at least about from 1 to 6 contiguous amino acids.
>
> For example, in a 17 amino acid CDRH3 region, structural amino acid positions are selected from the group consisting of the first N-terminal amino acid, the second N-terminal amino acid, at least one of the last 6 amino acids at the C-terminus of a heavy chain CDRH3 or mixtures thereof. The central portion has a length of 9 amino acids that can vary in sequence. In another embodiment, at least one structural amino acid position is one or both of the first two amino acid positions at the N-terminus of a heavy chain CDRH3. In another embodiment, said at

least one structural amino acid position is a third, fourth and/or sixth amino acid position counting from the C-terminus.

Once at least one structural amino acid position in a heavy chain CDRH3 is identified, a limited set of amino acids is selected for substitution at this position. The diversity at at least one structural amino acid position is limited to provide for maximal diversity while minimizing the structural perturbations. The number of amino acids that are substituted at a structural amino acid position is no more than about 1 to 7, about 1 to 4, or about 1 to 2 amino acids. In some embodiments, a variant amino acid at a structural amino acid position is encoded by one or more nonrandom codon sets. The nonrandom codon sets encode multiple amino acids for a particular positions, for example, about 1 to 7, about 1 to 4 amino acids or about 1 to 2 amino acids.

Therefore, the length of the N-terminus is from 1-4 amino acids, the length of the C-terminus is from 1-6 amino acids, and the length of the central portion is from 1 to 20 amino acids. The "structural" amino acid positions are the first N-terminal amino acid, the second N-terminal amino acid, and/or at least one of the six C-terminal amino acids.

New Objections

Specification

12. The disclosure is objected to because of the following informalities: because it contains embedded hyperlinks and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See the examples particularly. Applicants are respectfully requested to carefully review the entire specification for hyperlinks and/or other forms of browser-executable code. See MPEP § 608.01. Appropriate correction is required.

13. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any

errors of which applicant may become aware in the specification. Applicants are specifically requested to check the specification for any sequence which may require proper SEQ ID NOs:.

Claim Objections

14. Claims 105-107, 109-111, and 113-128 are objected to because of the following informalities: for consistency, utilizing either N-terminal and C-terminal or N terminal and C terminal is suggested (see claims 105-107, 109-111, 113, 115-120) and utilizing either semicolons or commas between a, b, and c (i.e. not both; see claim 105) is suggested. A space is required between "c)" and "a" (see claim 105). Claim 127 contains non-filamentous phage coat proteins in the Markush group. Claim 107 contains an amino acid sequence with four specifically defined amino acids without providing a proper SEQ ID NO:. Claim 110 contains an amino acid sequence with four specifically defined amino acids without providing a proper SEQ ID NO:. Claim 115 contains an amino acid sequence with four specifically defined amino acids without providing a proper SEQ ID NO:. Claim 128 contains an amino acid sequence with four specifically defined amino acids without providing a proper SEQ ID NO:. See MPEP § 2421.02. Claim 122 reads "at least one a variant" ("at least one variant" is suggested). Appropriate correction is required.

New Rejections

Claim Rejections - 35 USC § 112

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 105-107, 109-111, and 113-128 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **written description** rejection.

With regard to the written description requirement, the attention of the Applicant is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original) [The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)] (the case is referred to herein as "*Lilly*").

Additionally, it is noted that written description is legally distinct from enablement: "Although the two concepts are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co.*

Although directed to DNA compounds, this *Eli Lilly* holding would be deemed to be applicable to any compound or a generic of compounds; which requires a representative sample of compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the compound or generic(s). In this regard, applicant is further referred to *University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997); "Guidelines for Examination of Patent Applications Under the 35 USC 112, first paragraph, 'Written Description' Requirement" published in 1242 OG 168-178 (January 30, 2001); and *Univ. Of Rochester v G. D. Searle and Co.* 249 F. Supp. 2d 216 (W.D.N.Y. 2003) affirmed by the CAFC on February 13, 2004 (03-1304) publication pending.

Additionally, *Lilly* sets forth a two part test for written description:

A description of a genus of cDNA's may be achieved by means of a recitation of: a representative number of cDNA's, defined by nucleotide sequence, falling within the scope of the genus OR of a recitation of structural features common to the members of the genus. See *Regents of the University of California v. Eli Lilly & Co.* 119 F.3d 1559 (Fed. Cir. 1997) at 1569.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Additionally, Cf. University of Rochester v G.D. Searle & Co., Inc., Monsanto Company, Pharmacia Corporation, and Pfizer Inc., No. 03-1304, 2004 WL 260813 (Fed. Cir., Feb. 13, 2004) held that:

Regardless whether a compound is claimed per se or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods.

In the present instance, the specification discloses only limited examples that are not representative of the claimed genus of a "fusion protein" comprising "at least a portion of a filamentous phage coat protein" and a "CDRH3 comprising an N-terminal portion of 1 to 4 amino acid(s), a central or loop portion of 1 to 20 contiguous amino acids, and a C-terminal portion of 1 to 6 amino acids"; nor do the claims recite sufficient structural feature(s) which is(are) common to members of the genus sufficient to demonstrate possession of the genus. The instant claims define "at least a portion of a filamentous phage coat protein" as a portion which "provides for display of the fusion protein on the filamentous phage". The instant claims also state that some of the N-terminal and C-terminal amino acids are "structural". The claimed "at least a portion of a filamentous phage coat protein" is only defined by functional properties (e.g. "provides for display of the fusion protein on the filamentous phage") and the claimed "structural" amino acid positions are not defined by a structure. The CAFC held that a functional definition is insufficient to adequately describe a product, therefore, an adequate written description not based on a functional definition is necessary.

The Examiner further notes the present claims stated by Applicant are broader in scope that those that were held to be impermissible in *Lilly* because, unlike *Lilly*, Applicants' claims encompass a vast number of "fusion proteins" comprising a vast number of "at least a portion of a filamentous phage coat proteins" and a vast number of CDRH3s. Here, the Applicant claims a any portion of the filamentous phage coat protein and any CDRH3 to make the fusion protein (please refer to claim 105). The scope of these claims include a vast number of sequences because the specification and claims do not place any limit on the number of components (e.g. while the length of the CDRH3 is restricted, the amino acids utilized are not restricted; the length of the filamentous phage coat protein portion is not restricted) or the type of components (e.g. any amino acids, any portion of a filamentous phage coat protein). Furthermore, the specification and claims do not place any limit on the number of components, the types of components, or the manner in which the components might be connected to form a fusion protein wherein a "portion of a filamentous phage coat protein" is fused with a CDRH3. Therefore, Applicants are using an inadequately described "portion of a filamentous phage coat protein" and CDRH3 to inadequately describe the claimed "fusion protein". In addition, the "wherein the portion of the phage coat protein provides for display of the fusion protein on the filamentous phage" claim language (see claim 105) further exacerbates this problem because the conditions under which the portion of a filamentous phage coat protein will provide for display of the fusion protein on the filamentous phage are not specified. Consequently, there is no teaching that would allow a person of skill in the art to determine *a priori* that the Applicant was in possession of the full scope of the claimed invention at the time of filing because there is no common structural

attributes that can link together all of the claimed "fusion protein" or the portion of a filamentous phage coat protein fused with the CDRH3 to make the fusion protein.

While the general knowledge and level of skill in the art for antibodies and/or CDRH3 and phage display is high, this knowledge and level of skill does not supplement the omitted description because specific, not general, guidance is needed for the "portion of a filamentous phage coat protein" and CDRH3 which make up the fusion protein. Since the disclosure fails to describe the common attributes or characteristics that identify all of the members of the genus or even a substantial portion thereof, and because the genus is vast and highly variant (e.g. any CDRH3, any portion of a filamentous phage coat protein), the limited examples in the specification (please refer to the Examples in the Specification) is insufficient to teach the entire genus. Example 1 refers to the "C-terminal domain of gene III" and the CDRH3 of anti-her2 humanized antibody 4D5. Examples 2-6 refer to anti-her2 humanized antibody 4D5. Examples 7-8 and 13-14 refer to llama anti-HCG camelid monobody. Example 8 refers to the amino terminus of gene III. Examples 9-11 and 14 refer to protein A as an antigen source. Example 12 refers to human VEGF as an antigen source.

Further exacerbating the lack of written description is the necessity to have a specifically defined antigen or a specifically defined antibody when claiming an antibody product. For example, disclosure of an antigen fully characterized by its structure, formula, chemical name, physical properties, or deposit in a public depository provides an adequate written description of an antibody claimed by its binding affinity to that antigen. See *Noelle v. Lederman*, 355 F.3d 1343, 1349, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (holding there is a lack of written

descriptive support for an antibody defined by its binding affinity to an antigen that itself was not adequately described). See MPEP § 2163, section II.

The specification discloses only limited examples that are not representative of the claimed genus of a "fusion protein" comprising "at least a portion of a filamentous phage coat protein" and a CDRH3; nor do the claims recite sufficient structural feature(s) which is(are) common to members of the genus sufficient to demonstrate possession of the genus. Therefore, the teachings in the specification are general teachings relating without guidance as to the individual components of the product. In addition, there are numerous "fusion proteins" comprising "at least a portion of a filamentous phage coat protein" and a CDRH3 that could be employed in the invention with little direction or guidance for one of skill in the art to practice the claimed invention. The expedient statements in the specification do not relate to an adequate disclosure or how to make and use the claimed invention. Consequently, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to adequately describe the vast genus. Thus, Applicant does not appear to be in possession of the claimed genus.

17. Claims 105-107, 109-111, and 113-128 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **new matter** rejection.

Claim 105 recites that an N-terminal portion is 1 to 4 amino acids in which some or all amino acid positions are structural.

The specification as originally filed provided no implicit or explicit support for an N-terminal portion 1 to 4 amino acid residues in length wherein any one of the amino acids can be structural (i.e. only the first and second N-terminal amino acid can be structural).

Applicants are reminded that it is their burden to show where the specification supports any amendments to the disclosure. See MPEP § 714.02 and MPEP § 2163.06 I.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure.

18. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

19. Claims 105-107, 109-111, and 113-128 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 105 recites the limitation "the portion of the phage coat protein" in line 7 ("the portion of the filamentous phage coat protein" is suggested). There is insufficient antecedent basis for this limitation in the claim.

Claim 127 recites the limitation "the viral coat protein" in line 7 ("the filamentous phage coat protein" is suggested). There is insufficient antecedent basis for this limitation in the claim.

Claim 106 is indefinite because it is not clear if the cysteine residues must be present in the CDRH3 region only or if the cysteine regions are the normal cysteines found at the N- and C-terminus of the VH which produces the natural loop formation via disulfide bond present in naturally occurring antibodies.

Claims 105-107, 109-111, and 113-128 are indefinite because a normal CDRH3 is approximately 10 or 8-18 amino acids in length (portions of Abbas and Kabat will be provided as evidence if requested) while the presently claimed CDRH3 is 3-30 amino acids in length. Therefore, it is not clear if the N- and C-terminus are actually part of the adjacent framework regions or not.

Claim 120 is indefinite because it is not clear if the claim is referring to the C-terminal portion or to amino acids adjacent to the C-terminal portion (i.e. the fourth amino acid position **from** the C-terminus and the third amino acid position **from** the C-terminus).

Claim 121 is indefinite because applicants have not provided a Figure showing where residues 100g, 100h, 100i, 100j, 101, and 102 are in SEQ ID NO: 137 or provided the sequence

in the claims with markings regarding the specific residues. In addition, it is not clear if the residues indicated must be the same as in SEQ ID NO: 137 or if the residues are varied. What structure or sequence is required by the claim?

Claims 123-126 are indefinite because it is not clear how the residues are numbered (i.e. Kabat or some other numbering system).

Claim Rejections - 35 USC § 102

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

21. Claims 105-106, 113, 116, 117, 119, and 122-127 are rejected under 35 U.S.C. 102(b) as being anticipated by McCafferty et al. U.S. Patent 5,969,108 issued October 19, 1999.

For present claims 105-106, 113, 116, 117, 119, and 122-127, McCafferty et al. teach fusion proteins comprising filamentous phage coat protein including p3 and antibody domains comprising CDRH3 (CDRH3 naturally forms disulfide bond to produce VH loop structure; please refer to the entire specification particularly Figures 1, 3, 4b, 24b, 26a, 26b, 27, 28, 45, 52; columns 11-19; Examples).

Therefore, the teachings of McCafferty et al. anticipate the presently claimed invention.

Withdrawn Rejection

22. The rejection of claims 105-107, 109-111, and 113-128 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (i.e. new matter).

Maintained Rejections

Claim Rejection(s) – 35 USC § 102

23. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

24. Claims 105-107, 109-111, and 113-128 are rejected under 35 U.S.C. 102(a) as being anticipated by **Bond et al** (2003 J. Mol. Biol. 332:643-655 – provided by applicants in the IDS).

For present claims 105-107, 109-111, and 113-128, **Bond et al** teach, through out the document and especially the abstract, structural contributions made by CDR3 loops in camelid V_HH domains.

Said CDR3 loops in camelid V_HH domains are taken as a CDRH3 scaffold, as set forth in claim 105 and defined in paragraph 0014 of the present published application (i.e. CDRH3 is the CDR3 of the heavy chain). Bond et al teach construction of a llama anti-human chorionic gonadotropin (alphaHCG) V_HH fused to phage coat protein P3 on p 652, first paragraph. Bond et al teach in the paragraph bridging pp 644-645, the anti-alphaHCG structure comprises Trp 100 packing against Phe 37 and the aliphatic portion of Arg 45. Said Phe 37 and Arg 45 are taken as two structural amino acid positioned in the N terminal portion of claim 105. Said Trp 100 is taken as one structural amino acid positioned in the C terminal portion of claim 105. Bond et al teach on p 645 last paragraph insertions into said anti-alphaHCG at the short seven residue CDR3 loop, therein accommodating insertion of a central portion, reading on claim 105.

Bond et al teach in figure 1, camelid V_HH domains may comprise a disulfide bond between residues Cys 33 and Cys 109, reading on claim 106.

Bond et al teach in the table in figure 4a, a V_HH bearing a 17 residue insert comprising the sequence RIGR-...-WVTW (elected species) as an insert, reading on: R-L/I/MA_3-R when A_3 is Gly, as set forth in claim 107; the R-I of claim 109; the W-V of claim 111; C terminal portion being 4 amino acids of claim 113; center portion being 9 amino acids of claim 114; R-L/I/MA_3-R when A_3 is Gly and W-A7-A8-A9-A10-A11, wherein A7-11 can be any amino acid as set forth in claim 115.

Bond et al teach on p 649 second paragraph and figure 3b, shotgun alanine scanning as indicative of RI and WV being structural in said RIGR...WVTW insert, as set forth in claim 116-120.

Said WV is in positions 100i and 100j, according to figure 4a of Bond et al, as set forth in claim 121. Said figure 4a of Bond et al includes species bearing a central portion having at least one variant amino acid encoded by a non-random codon set as set forth in claim 122.

Said Phe 37 reads on the phenylalanine of claim 124 and hydrophobic residue of claim 123. Said Arg 45 reads on the arginine of claims 125 and 123. Bond et al teach Threonine at position 91 in figure 2, which appears to be in another framework region, reading on claim 126.

Said RIGR-...WVTW insert of Bond et al in figure 4a is 17 residues and reads on claim 128 when A1 is R, A2 is I, A3 is G, A4 is R, n is 9, A6 is S, A7 is W, A8 is V, A9 is T and A10 is W.

Therefore, the presently claimed invention is anticipated by the teachings of Bond et al.

Arguments and Response

25. Applicants' arguments directed to the rejection under 35 USC 102 (a) as being anticipated by Bond et al. for claims 105-107, 109-111, and 113-128 were considered but are not persuasive for the following reasons.

Applicants contend that the presently claimed invention has a priority date of January 16, 2003 or July 18, 2003 (i.e. earlier than the publication date of the Bond et al. reference).

Applicants' arguments are not convincing since the teachings of Bond et al. anticipate the fusion protein of the instant claims. The presently claimed invention has a priority date of January 16, 2004.

Claim Rejection(s) – Double Patenting

26. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

27. Claims 105-107, 109-111, and 113-128 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22, 25, 26, 30,

31, 35-37, and 48-50 of copending Application No. 11/102502 (referred to as '502) in view of **Sidhu et al** (2000 J. Mol. Biol. 296:487-495 – IDS entry 9/27/2004) and evidenced by Bond et al (2003 J. Mol. Biol. 332:643-655 – IDS entry 9/27/2004) for the reasons set forth in the office action mailed 12/29/2006.

Arguments and Response

28. Applicants' arguments directed to the rejection on the ground of nonstatutory obviousness-type double patenting as being unpatentable over copending application 11/102,502 for claims 105-107, 109-111, and 113-128 were considered but are not persuasive for the following reasons.

Applicants request that the rejection be held in abeyance.

While a request may be made that objections or requirements as to form not necessary to further consideration of the claims be held in abeyance until allowable subject matter is indicated, the present is a rejection and will not be held in abeyance (see MPEP § 714.02).

New Rejection

Double Patenting

29. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

30. Claims 105, 106, 113, 114, 116-120, and 122-126 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-68 of U.S. Patent No. 7,521,541. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed invention and the invention as claimed in U.S. Patent 7,521,541 are drawn to CDRH3 fused to a phage coat protein (see claim 8).

Interview Request

31. Applicants are respectfully requested to telephone the current examiner of record to set up a mutually convenient time for an interview.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMBER D. STEELE whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Primary Examiner, Art Unit 1639

August 17, 2009